DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 22, 2008, has been entered.

1. The amendment filed June 3, 2009, is acknowledged and has been entered. Claims 78, 139, and 156-158 have been canceled. Claims 69, 76, 77, 79, 124-127, 129, 130, 137, 140, 153, 159, 160, 170-172, and 186 have been amended. Claims 191-196 have been added.

2. The amendment filed September 24, 2009, is acknowledged and has been entered. Claims 130, 191, and 194 have been canceled. Claims 69 and 124-127 have been amended.

Response to Amendment

3. The amendment filed on September 24, 2009, is considered non-compliant because it fails to meet the requirements of 37 CFR § 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). However, in order to advance prosecution[1], rather than mailing a Notice of Non-Compliant Amendment, Applicant is advised of the following deficiency in the listing of the claims:

The amendment is non-compliant because claim 172, which is correctly identified as "previously presented", is marked to show a change already made to the claim by the prior filed amendment.

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[1] See M.P.E.P. § 714.03.

Terminal Disclaimer

4. The terminal disclaimer filed on September 24, 2009, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of Patent No. 7,514,078 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Grounds of Objection and Rejection Withdrawn

5. Applicant's amendment and/or arguments and the terminal disclaimer filed September 24, 2009, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed November 21, 2007.

Examiner's Amendment

6. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

7. Authorization for this examiner's amendment was given in a telephone interview with Isaac A. Hubner on September 30, 2009.

8. The application has been amended as follows:

In the claims:

The following set of claims has replaced prior set of claims filed September 24, 2009:

Claims 1-68. (Canceled)

Claim 69. (Currently Amended) A method of treating prostate cancer comprising:

providing a monoclonal antibody or antigen binding portion thereof which binds to prostate specific membrane antigen (PSMA) and competes for binding to PSMA with a monoclonal antibody selected from the group consisting of a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12101, a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12127, and a monoclonal antibody produced by a hybridoma with an ATCC accession number ~~HB-1216~~ HB-12126 wherein the antibody or antigen binding portion thereof is conjugated to a cytotoxic drug; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat prostate cancer.

Claim 70. (Previously Presented) The method according to claim 69, wherein the prostate cancer is metastatic prostate cancer.

Claim 71. (Previously Presented) The method according to claim 70, wherein the metastatic prostate cancer involves a bone marrow or a lymph node metastasis.

Claim 72. (Previously Presented) The method according to claim 69, wherein the administering is carried out parenterally.

Claim 73. (Previously Presented) The method according to claim 69, wherein the administering is carried out intravenously.

Claim 74. (Previously Presented) The method according to claim 69, wherein the administering is carried out by intracavitary instillation.

Claim 75. (Cancelled)

Claim 76. (Previously Presented) The method according to claim 69, wherein the monoclonal antibody or antigen binding portion thereof is administered following a prostatectomy.

Claim 77. (Previously Presented) The method according to claim 69, wherein the monoclonal antibody or antigen binding portion binds live cells.

Claim 78. (Cancelled)

Claim 79. (Currently Amended) The method according to claim 69, wherein the monoclonal antibody provided is produced by a hybridoma with an ATCC accession number HB- 12101.

Claims 80-123. (Cancelled)

Claim 124. (Currently Amended) A method of treating prostate cancer comprising:

providing a monoclonal antibody or antigen binding portion thereof which binds to prostate specific membrane antigen (PSMA) and competes for binding to PSMA with a monoclonal antibody selected from the group consisting of [[an]] a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12101, a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12127, and a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12126, wherein the antibody is labeled with the radiolabel ^{90}Y; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat prostate cancer.

Claim 125. (Previously Presented) A method of treating prostate cancer comprising:

providing a monoclonal antibody or antigen binding portion thereof which binds to prostate specific membrane antigen (PSMA) and competes for binding to PSMA with a monoclonal antibody selected from the group consisting of a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12101, a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12127, and a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12126, wherein the antibody is labeled with a radiolabel, and wherein the radiolabel is a beta- or gamma-emitter; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat prostate cancer.

Claim 126. (Previously Presented) A method of treating prostate cancer comprising:

providing a monoclonal antibody or antigen binding portion thereof which binds to prostate specific membrane antigen (PSMA) and competes for binding to PSMA with a monoclonal antibody selected from the group consisting of a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12101, a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12127, and a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12126, wherein the antibody is bound to a cytotoxic drug of bacterial origin; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat prostate cancer.

Claim 127. (Previously Presented) A method of treating prostate cancer comprising:

providing a monoclonal antibody or antigen binding portion thereof which binds to prostate specific membrane antigen (PSMA) and competes for binding to PSMA with a monoclonal antibody selected from the group consisting of a monoclonal antibody

produced by a hybridoma with an ATCC accession number HB-12101, a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12127, and a monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12126, wherein the antibody is bound to a cytotoxic drug of plant origin; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat prostate cancer.

Claim 128. (Cancelled)

Claim 129. (Previously Presented) The method according to claim 69, wherein the monoclonal antibody or antigen binding portion thereof competes for binding to PSMA with the monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12126.

Claims 130-136. (Cancelled)

Claim 137. (Previously Presented) The method according to claim 69, 125, 126 or 127, wherein the monoclonal antibody or antigen binding portion thereof is internalized with the PSMA.

Claim 138. (Previously Presented) The method according to claim 69, 125, 126 or 127, wherein the antigen binding portion is selected from the group consisting of a Fab fragment, a F(ab')2 fragment, and a Fv fragment.

Claim 139. (Cancelled)

Claim 140. (Previously Presented) The method according to claim 69, wherein the cytotoxic drug is selected from the group consisting of a therapeutic drug, a compound emitting radiation, a molecule of plant, fungal, or bacterial origin, a biological protein, and a mixture thereof.

Claim 141. (Currently Amended) The method according to claim [[140]] 69, wherein the cytotoxic drug is a compound emitting radiation.

Claim 142. (Previously Presented) The method according to claim 141, wherein the compound emitting radiation is an alpha-emitter.

Claim 143. (Previously Presented) The method according to claim 142, wherein the alpha-emitter is selected from the group consisting of ^{212}Bi, ^{213}Bi, and ^{211}At.

Claim 144. (Previously Presented) The method according to claim 141, wherein the compound emitting radiation is a beta-emitter.

Claim 145. (Previously Presented) The method according to claim 144, wherein the beta-emitter is ^{186}Re.

Claim 146. (Previously Presented) The method according to claim 144, wherein the beta-emitter is ^{90}Y.

Claim 147. (Previously Presented) The method according to claim 141, wherein the compound emitting radiation is a gamma-emitter.

Claim 148. (Previously Presented) The method according to claim 147, wherein the gamma-emitter is ^{131}I.

Claim 149. (Cancelled)

Claim 150. (Currently Amended) The method according to claim [[140]] 69, wherein the cytotoxic drug is a molecule of bacterial origin.

Claim 151. (Currently Amended) The method according to claim [[140]] 69, wherein the cytotoxic drug is a molecule of plant origin.

Claim 152. (Currently Amended) The method according to claim [[140]] 69, wherein the cytotoxic drug is a biological protein.

Claim 153. (Previously Presented) The method according to claim 69, wherein the monoclonal antibody or antigen binding portion thereof further comprises a label.

Claim 154. (Previously Presented) The method according to claim 153, wherein the label is selected from the group consisting of a biologically-active enzyme label, and a radiolabel.

Claim 155. (Previously Presented) The method according to claim 154, wherein the label is a radiolabel selected from the group consisting of ^{111}In, ^{99m}Tc, ^{32}P, ^{125}I, ^{131}I, ^{14}C, ^{3}H and ^{188}Rh.

Claim 156-158. (Cancelled)

Claim 159. (Currently Amended) The method according to claim 69, 125, 126 or 127, wherein the monoclonal antibody or antigen binding portion thereof administered to the subject is in a composition further comprising a pharmaceutically acceptable carrier, excipient, or stabilizer.

Claim 160. (Previously Presented) The method according to claim 69, 125, 126 or 127 wherein the monoclonal antibody or antigen binding portion thereof is administered in conjunction with a second therapeutic modality.

Claim 161. (Previously Presented) The method according to claim 160, wherein the second therapeutic modality is selected from the group consisting of surgery, radiation, chemotherapy, immunotherapy and hormone replacement.

Claim 162. (Previously Presented) The method according to claim 161, wherein the hormone replacement comprises treatment with estrogen or an anti-androgen agent.

Claim 163. (Previously Presented) The method according to claim 162, wherein the anti-androgen agent is an agent which blocks or inhibits the effects of testosterone.

Claim 164. (Previously Presented) The method according to claim 126, wherein the prostate cancer is metastatic prostate cancer.

Claim 165. (Previously Presented) The method according to claim 164, wherein the metastatic prostate cancer involves a bone marrow or a lymph node metastasis.

Claim 166. (Previously Presented) The method according to claim 126, wherein the administering is carried out parenterally.

Claim 167. (Previously Presented) The method according to claim 126, wherein the administering is carried out intravenously.

Claim 168. (Previously presented) The method according to claim 126, wherein the administering is carried out by intracavitary instillation.

Claim 169. (Cancelled)

Claim 170. (Previously Presented) The method according to claim 126, wherein the monoclonal antibody or antigen binding portion thereof is administered following a prostatectomy.

Claim 171. (Previously Presented) The method according to claim 126, wherein the monoclonal antibody or antigen binding portion binds live cells.

Claim 172. (Currently Amended) The method according to claim 126, wherein the monoclonal antibody provided is produced by a hybridoma with an ATCC accession number HB- 12101.

Claim 173-185. (Cancelled)

Claim 186. (Previously Presented) The method according to claim 126, wherein the monoclonal antibody or antigen binding portion thereof competes for binding to PSMA with the monoclonal antibody produced by a hybridoma with an ATCC accession number HB-12126.

Claim 187 -189. (Cancelled)

Claim 190. (Currently Amended) The method according to claim 69, 124, 125, 126, or 127, wherein the method of treating prostate cancer is a method that prevents the progression of prostate cancer or delays the progression of prostate cancer in the subject.

Claim 191. (Cancelled)

Claim 192. (Currently Amended) The method according to claim 69, wherein the monoclonal antibody provided is produced by a hybridoma with an ATCC accession number HB-12127.

Claim 193. (Currently Amended) The method according to claim 69, wherein the monoclonal antibody provided is produced by a hybridoma with an ATCC accession number HB-12126.

Claim 194. (Cancelled)

Claim 195. (Currently Amended) The method according to claim 126, wherein the monoclonal antibody provided is produced by a hybridoma with an ATCC accession number HB-12127.

Claim 196. (Currently Amended) The method according to claim 126, wherein the monoclonal antibody provided is produced by a hybridoma with an ATCC accession number HB-12126.

Examiner's Statement of Reasons for Allowance

9. The following is an examiner's statement of reasons for allowance:

Support for the amendment to the claims is found throughout the specification, including the claims, as originally filed. Claims 69 and 124 have been amended to correct typographical errors; and claims 79, 141, 150-152, 159, 172, 190, 192, 193, 195, and 196 have been amended to more clearly claim the subject matter that is regarded as the invention.

The claims are drawn to a method of treating prostate cancer comprising administering to a subject under conditions effective to treat prostate cancer an monoclonal antibody or antigen binding portion thereof that binds to PSMA and competes for binding to PSMA with another monoclonal antibody selected from the group consisting of a monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12101, a monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12127, and a monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12126, wherein the monoclonal

antibody or antigen binding portion thereof administered to the subject is conjugated to a cytotoxic drug.

The specification discloses that the monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12101 is the monoclonal antibody designated E99; see, e.g., Table 1 at page 19 of the specification, as originally filed. The monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12127 is the monoclonal antibody designated J533; and the monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12126 is designated J591.

The specification discloses that each of monoclonal antibodies E99, J533, and J591 bind to PSMA and compete for binding to PSMA with one another; see, e.g., page 38, lines 11-16 of the specification, as originally filed. Another antibody produced by a hybridoma deposited under ATCC accession number HB-12109, which is designated monoclonal antibody J415, is also described in this application; but no other antibody described therein is described as capable of competing for binding to PSMA with monoclonal antibody J415 and notably the claims are not directed to a monoclonal antibody that is capable of competing for binding to PSMA with monoclonal antibody J415.

The prior does not teach or fairly suggest the claimed method of treating prostate cancer, which comprises administering to a subject under conditions effective to treat prostate cancer an immunoconjugate comprising a cytotoxic drug, which is conjugated to a monoclonal antibody or antigen binding portion thereof that binds to PSMA and competes for binding to PSMA with another monoclonal antibody selected from the group consisting of a monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12101 ("E99"), a monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12127 ("J533"), and a monoclonal antibody produced by a hybridoma having the ATCC accession number HB-12126 ("J591"). Although the prior art teaches a plurality of monoclonal antibodies that bind to PSMA, or more particularly the extracellular domain of the molecule, the Office has no factual evidence that any of the monoclonal antibodies described by the prior art are effective

to inhibit binding of any of monoclonal antibodies E99, J533 and J591, as each of E99, J533, and J591 is disclosed as capable of doing in the competition studies described by Example 10 of this application (pages 37-39 of the specification, as originally filed).

10. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

11. Claims 69-74, 76, 77, 79, 124-127, 129, 137, 138, 140-148, 150-155, 159-168, 170-172, 186, 190, 192, 193, 195, and 196 have been allowed.

12. Claims 69-74, 76, 77, 79, 124-127, 129, 137, 138, 140-148, 150-155, 159-168, 170-172, 186, 190, 192, 193, 195, and 196 have been renumbered as claims 1-50, respectively.

13. The art made of record and not relied upon is considered pertinent to Applicant's disclosure. Li et al (*Prostate Cancer Prostatic Dis.* 2002; **5** (1): 36-46) teaches *in vitro* and preclinical targeted alpha therapy of human prostate cancer with Bi-213 labeled J591 antibody against PSMA.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

slr
September 30, 2009